

**AMENDMENT AND RESPONSE TO OFFICE ACTION**  
U.S.S.N. 10/612,463

**Remarks**

The present invention is directed to kits for intravesicular instillation of resiniferatoxin, tinyatoxin, 20-homovanillyl-mezerein or 20-homovanillyl-12-deoxyphorbol-13-phenylacetate. Claim 4 has been previously cancelled. Claim 1 has been amended. By entry of this amendment, claims 1-3 and 5-13 are pending.

**Rejections under 35 U.S.C. §103**

Claims 1, 5 and 6-7 are rejected under 35 U.S.C. §103 for lacking novelty over Craft et al, Physiology & Behavior 56(3):479-486, 1994 (“Craft”) in view of Nordhauser et al., Sterilization of Drugs and Devices: Technologies for the 21<sup>st</sup> Century, Forward, 1998 (“Nordhauser”). Applicants respectfully traverse the rejection.

The claims are directed to a kit comprising a sterile unit dose of a therapeutic compound that is compatible with bladder mucosa and does not cause meaningful pain or irritation when administered. The claims have been amended to recite that the unit dose is sterile. Craft administers RTX to rats for only a 24 hour period before the experiment is concluded so Craft would not have any regard for sterility of the RTX solutions like one would have in human treatment.

The specification also teaches that the formulations and kits disclosed therein are compatible with bladder mucosa and do not cause meaningful pain or irritation when administered. Since the therapeutic compositions disclosed by Craft all cause significant pain and irritation as evidenced by the frequent peritoneal licking, Craft fails to satisfy all elements of the claims. The Examiner asserts that this element relates to an intended use of the kit. Applicants respectfully disagree and respectfully assert that this claim element is a property of the concentration in the claimed kit.

As was recently clarified by the CAFC in In re Sullivan, “[t]he issue here is not whether a claim recites a new use, but whether the subject matter of the claim possesses an unexpected use. That unexpected property is relevant...” (In re Sullivan, 498 F.3d 1345 (Fed. Cir. 2007)). Citing In re Papesch, the Court iterated that “From a standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing... There is no basis in law for

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ignoring any property in making such a comparison". (*In re Papesch*, 315 F.2d 381, 391 (CCPA 1963)). While mere statement of an intended use can not render an old composition patentable, the unexpected property of not causing meaningful pain or irritation to the patient when administered can not be ignored. Craft fails to suggest that the concentration would have the property of not causing meaningful pain or irritation to the patient when administered. The RTX references cited by the Examiner fail to teach this property of not causing meaningful pain or irritation to the patient when administered, which is now recited in the claims. One of ordinary skill would not have been motivated to combine the cited references or modify the teachings of Craft to achieve the result of providing a concentration of RTX without causing meaningful pain or irritation to the patient when administered. Therefore the cited references alone, or in combination fail to render the claimed kit obvious. Withdrawal of this rejection is respectfully requested.

Claims 2 and 3 have been rejected under 35 U.S.C. §103 for being obvious over Craft et al, *Physiology & Behavior* 56(3):479-486, 1994 (“Craft”) in view of Nordhauser et al., *Sterilization of Drugs and Devices: Technologies for the 21<sup>st</sup> Century, Forward*, 1998 (“Nordhauser”) and U.S. Patent No. 4,939,149 (“Blumberg”). Applicants respectfully traverse the rejection.

Craft is discussed above. Blumberg fails to disclose that RTX can be formulated such that the final administered composition is compatible with bladder mucosa and does not cause meaningful pain or irritation when administered.

Blumberg teaches that resiniferatoxin is an extremely irritant diterpene. Even the examples of the specification necessitate the use of ether anaesthesia to avoid unnecessary pain (column 6, line 34). One of ordinary skill would conclude, when faced with the teachings of Blumberg, that RTX would cause pain and burning sensations when administered. Blumberg actually teaches away from the Applicants’ invention that low doses of RTX in humans treats urinary incontinence without causing pain or burning sensations that are associated with CAP treatment or higher concentrations of RTX that are seen in Blumberg. (Specification paragraphs 14). The claimed kit is inventive by providing a dosage that treats urinary incontinence without

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pain and burning sensations. This feature could not possibly be obvious in view of the teachings of Blumberg that teach how irritating RTX is. Even Craft teaches that RTX administration in rats results in a visceral nociceptive response. (Craft, page 479, second column). As such, neither Craft or Blumberg provides sufficient motivation to arrive at the claimed kits for providing a therapeutic dosage of RTX as claimed and fail to render the claimed kits obvious. The Examiner asserts that this element relates to an intended use of the kit. Applicants respectfully disagree and respectfully assert that this claim element is a property of the concentration in the claimed kit.

As was recently clarified by the CAFC in In re Sullivan, “[t]he issue here is not whether a claim recites a new use, but whether the subject matter of the claim possesses an unexpected use. That unexpected property is relevant...” (In re Sullivan, 498 F.3d 1345 (Fed. Cir. 2007)). Citing In re Papesch, the Court iterated that “From a standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing... There is no basis in law for ignoring any property in making such a comparison”. (In re Papesch, 315 F.2d 381, 391 (CCPA 1963)). While mere statement of an intended use can not render an old composition patentable, the unexpected property of not causing meaningful pain or irritation to the patient when administered can not be ignored. Craft fails to suggest that the concentration would have the property of not causing meaningful pain or irritation to the patient when administered. The RTX references cited by the Examiner fail to teach this property of not causing meaningful pain or irritation to the patient when administered, which is now recited in the claims. One of ordinary skill would not have been motivated to combine the cited references or modify the teachings of Craft to achieve the result of providing a concentration of RTX without causing meaningful pain or irritation to the patient when administered. Therefore the cited references alone, or in combination fail to render the claimed kits obvious. Withdrawal of this rejection is respectfully requested.

Claims 8-10 have been rejected under 35 U.S.C. §103 for being obvious over Craft et al, Physiology & Behavior 56(3):479-486, 1994 (“Craft”) in view of Nordhauser et al., Sterilization of Drugs and Devices: Technologies for the 21<sup>st</sup> Century, Forward, 1998 (“Nordhauser”) and U.S. Patent No. 2,182,075 (“Ebert”). Applicants respectfully traverse the rejection.

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Craft has been discussed above. Ebert fails to make up for the deficiencies of Craft and therefore fails to render the claimed kits obvious. The Examiner asserts that this element relates to an intended use of the kit. Applicants respectfully disagree and respectfully assert that this claim element is a property of the concentration in the claimed kit.

As was recently clarified by the CAFC in *In re Sullivan*, “[t]he issue here is not whether a claim recites a new use, but whether the subject matter of the claim possesses an unexpected use. That unexpected property is relevant...” (*In re Sullivan*, 498 F.3d 1345 (Fed. Cir. 2007)). Citing *In re Papesch*, the Court iterated that “From a standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing... There is no basis in law for ignoring any property in making such a comparison”. (*In re Papesch*, 315 F.2d 381, 391 (CCPA 1963)). While mere statement of an intended use can not render an old composition patentable, the unexpected property of not causing meaningful pain or irritation to the patient when administered can not be ignored. Craft fails to suggest that the concentration would have the property of not causing meaningful pain or irritation to the patient when administered. The RTX references cited by the Examiner fail to teach this property of not causing meaningful pain or irritation to the patient when administered, which is now recited in the claims. One of ordinary skill would not have been motivated to combine the cited references or modify the teachings of Craft to achieve the result of providing a concentration of RTX without causing meaningful pain or irritation to the patient when administered. Therefore the cited references alone, or in combination fail to render the claimed kits obvious. Withdrawal of this rejection is respectfully requested.

Claims 11-13 are rejected under 35 U.S.C. 103(a) as being obvious over Craft et al., Nordhauser et al. and Blumberg as applied to claims 1-3, 5, and 6-7 above, and further in view of Mookherjee et al (U.S. Patent 4145354 A). Applicants respectfully traverse the rejection as it applies to the amended claims

Claim 11 has been amended to recite that the dosage in the kit does not cause meaningful pain or irritation to the patient. This added claim element is a property of the concentration in the claimed kit.

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As was recently clarified by the CAFC in In re Sullivan, “[t]he issue here is not whether a claim recites a new use, but whether the subject matter of the claim possesses an unexpected use. That unexpected property is relevant...” (In re Sullivan, 498 F.3d 1345 (Fed. Cir. 2007)). Citing In re Papesch, the Court iterated that “From a standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing... There is no basis in law for ignoring any property in making such a comparison”. (In re Papesch, 315 F.2d 381, 391 (CCPA 1963)). While mere statement of an intended use can not render an old composition patentable, the unexpected property of not causing meaningful pain or irritation to the patient when administered can not be ignored. Craft fails to suggest that the concentration would have the property of not causing meaningful pain or irritation to the patient when administered. The RTX references cited by the Examiner fail to teach this property of not causing meaningful pain or irritation to the patient when administered, which is now recited in the claims. One of ordinary skill would not have been motivated to combine the cited references or modify the teachings of Craft to achieve the result of providing a concentration of RTX without causing meaningful pain or irritation to the patient when administered. Therefore the cited references alone, or in combination fail to render the claimed kits obvious. Withdrawal of this rejection is respectfully requested.

**Double Patenting**

Claims 1-3 have been rejected for obviousness-type double patenting over U.S. Patent 6,630,515. Applicants file herein a terminal disclaimer to overcome this rejection. Withdrawal of this rejection is respectfully requested.

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**Conclusions**

Applicants submit that the response herein provides a complete response to the Office Action dated August 5, 2008.

If the Examiner believes there are other issues that may be resolved by telephone interview, or that there are any informalities remaining in the application that may be corrected by Examiner's Amendment, a telephone call to the undersigned is respectfully solicited.

No additional fees are believed due, however the Commissioner is hereby authorized to charge any additional fees that may be required, or credit any overpayment of fees to Deposit Account number 11-0980.

Respectfully submitted,



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